

CLAIM AMENDMENTS:

Claims 1, 9-11, 13, 14, 16, 17, 19, 21, 26-37, 39, 40, 42 and 43 have been amended. The following listing of claims will replace all prior versions and listings, of claims in this Application.

Listing of Claims:

Claim 1 (Currently amended): A formulated liposome for incorporating a high content of hydrophobic substances therein, comprising:

a first phospholipid which is selected from the group consisting of a hydrogenated naturally-occurring phospholipid [[or]] and a saturated phospholipid having long carbon chains $-(CH_2)_n-$, in which n is at least 14), and which has a phase transition temperature T_{g1} ranging between 40 and 74°C;

a second phospholipid which is selected from the group consisting of an unsaturated phospholipid [[or]] and a saturated phospholipid having short carbon chains $-(CH_2)_n-$, in which n is at most 14), and which has a phase transition temperature T_{g2} ranging between -30 and 10°C;

liposome-forming materials effective to form a liposome in which the first phospholipid and the second phospholipid coexist in two immiscible phases and create several discontinuous regions, and in which a molar ratio of the first phospholipid to the second phospholipid is at least 3:16; and

one or more hydrophobic substances incorporated in the liposome in an amount of at least 20 mole% to form the formulated liposome, wherein a drug delivery temperature T_1 and a drug storage temperature T_2 are chosen at specified ranges subject to an order of $T_{g1} > T_1 > T_2 > T_{g2}$, and wherein the formulated liposome has an incorporation efficiency which remains at at least about 70% of incorporation efficiency for six months or more.

Claim 2 (Previously presented): The formulated liposome according to claim 1, wherein the phase transition temperature of the first phospholipid ranges between 50 and 65°C, and the phase transition temperature of the second phospholipid ranges between -20 and 4°C.

Claim 3 (Previously presented): The formulated liposome according to claim 1, wherein the first phospholipid is selected from the group consisting of phosphatidyl choline (PC), phosphatidyl glycerol (PG), phosphatidyl serine (PS), phosphatidyl acid (PA) and phosphatidyl ethanolamine (PE).

Claim 4 (Previously presented): The formulated liposome according to claim 3, wherein the first phospholipid is selected from the group consisting of hydrogenated egg phosphatidyl choline (HEPC), hydrogenated soy phosphatidyl choline (HSPC), dipalmitoyl phosphatidyl choline (DPPC) and distearoyl phosphatidyl choline (DSPC), diarachidoyl phosphatidyl choline, dimyristoyl phosphatidyl ethanolamine (DMPE), dipalmitoyl phosphatidyl ethanolamine (DPPE), distearoyl phosphatidyl ethanolamine (DSPE), dipalmitoyl phosphatidyl glycerol (DPPG), distearoyl phosphatidyl glycerol, dimyristoyl phosphatidyl acid (DMPA), dipalmitoyl phosphatidyl acid (DPPA), dipalmitoyl phosphatidyl serine (DPPS), and distearoyl phosphatidyl serine (DSPS).

Claim 5 (Previously presented): The formulated liposome according to claim 1, wherein the second phospholipid is selected from the group consisting of phosphatidyl choline (PC), phosphatidyl glycerol (PG), phosphatidyl serine (PS), phosphatidyl acid (PA) and phosphatidyl ethanolamine (PE).

Claim 6 (Previously presented): The formulated liposome according to claim 5, wherein the second phospholipid is selected from the group consisting of egg phosphatidyl choline (EPC), soy phosphatidyl choline (SPC), oleoyl palmitoyl phosphatidyl choline, dioleoyl phosphatidyl choline, dipetroselinoyl phosphatidyl choline, dipalmitelaidoyl phosphatidyl choline, dioleoyl phosphatidyl ethanolamine, dioleoyl phosphatidyl serine, dilauroyl phosphatidyl choline (DLPC), diundecanoyl phosphatidyl choline, didecanoyl phosphatidyl ethanolamine, and dinonanoyl phosphatidyl ethanolamine.

Claim 7 (Previously presented): The formulated liposome according to claim 1, wherein the hydrophobic substances are one or more hydrophobic pharmaceutical compounds.

Claim 8 (Previously presented): The formulated liposome according to claim 7, wherein the one or more hydrophobic pharmaceutical compound is paclitaxel.

Claim 9 (Currently amended): The formulated liposome according to claim 8, wherein the paclitaxel is incorporated with a drug/lipid ratio ranging from at least 20 ~~about 0.5~~ mole% to 25 mole%.

Claim 10 (Currently amended): The formulated liposome according to claim 9, wherein the paclitaxel is incorporated with a drug/lipid ratio ranging from at least 20 ~~about 0.5~~ mole% to 25 mole% when the first phospholipid is hydrogenated egg phosphatidyl choline (HEPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 11 (Currently amended): The formulated liposome according to claim 9, wherein the paclitaxel is incorporated with a drug/lipid ratio ranging from at least 20 ~~about 0.5~~ mole% to 25 mole% when the first phospholipid is hydrogenated soy phosphatidyl choline (HSPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 12 (Previously presented): The formulated liposome according to claim 7, wherein the hydrophobic pharmaceutical compound is retinoic acid.

Claim 13 (Currently amended): The formulated liposome according to claim 12, wherein the retinoic acid is incorporated with a drug/lipid ratio ranging from at least 20 ~~about 0.5~~ mole% to 40 mole%.

Claim 14 (Currently amended): The formulated liposome according to claim 13, wherein the retinoic acid is incorporated with a drug/lipid ratio ranging from at least 20 ~~about 10~~ mole% to 40 mole% when the first phospholipid is hydrogenated soy phosphatidyl choline (HSPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 15 (Previously presented): The formulated liposome according to claim 7, wherein the hydrophobic pharmaceutical compound is camptothecin.

Claim 16 (Currently amended): The formulated liposome according to claim 15, wherein the camptothecin is incorporated with a drug/lipid ratio ranging from at least 20 ~~about~~ 0.5 mole% to 30 mole%.

Claim 17 (Currently amended): The formulated liposome according to claim 16, wherein the camptothecin is incorporated with a drug/lipid ratio ranging from at least 20 ~~about~~ 5 mole% to 30 mole% when the first phospholipid is hydrogenated egg phosphatidyl choline (HEPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 18 (Previously presented): The formulated liposome according to claim 7, wherein the hydrophobic pharmaceutical compound is selected from the group consisting of paclitaxel retinoic acid, and camptothecin.

Claim 19 (Currently amended): The formulated liposome according to claim 1, wherein the liposome-forming materials are selected from the group consisting of hydrophilic polymer-modified lipids, cholesterol, ~~cholesterol derivatives~~, antioxidant, and mixtures thereof.

Claim 20 (Previously presented): The formulated liposome according to claim 19, wherein the hydrophilic polymer-modified lipid is methoxy polyethylene glycol-distearoyl phosphatidyl ethanolamine (MPEG-DSPE).

Claim 21 (Currently amended): A formulated liposome for incorporating a high content of hydrophobic substances therein, comprising:

a first phospholipid which is optionally a phosphatidyl choline, which is selected from the group consisting of a hydrogenated naturally-occurring phospholipid [[or]] and a saturated phospholipid having long carbon chains $-(CH_2)_n-$, in which n is at least 14, and which has a phase transition temperature T_{g1} ranging between 40 and 74°C ;

a second phospholipid which is optionally a phosphatidyl choline, which is selected from the group consisting of an unsaturated phospholipid [[or]] and a saturated phospholipid having short carbon chains $-(CH_2)_n-$, in which n is at most 14, and which has a phase transition temperature T_{g2} ranging between -30 and 10°C;

liposome-forming materials effective to form a liposome in which the first phospholipid and the second phospholipid coexist in two immiscible phases and create several discontinuous regions; and

one or more hydrophobic substances incorporated in the liposome in an amount of at least 20 mole% to form the formulated liposome, wherein a drug delivery temperature T_1 and a drug storage temperature T_2 are chosen at specified ranges subject to an order of $T_{g1} > T_1 > T_2 > T_{g2}$, and wherein the formulated liposome has an incorporation efficiency which remains at at least about 70% of incorporation efficiency for six months or more.

Claim 22 (Previously presented): The formulated liposome according to claim 21, wherein the phase transition temperature of the first phospholipid ranges from 50 to 65°C, and the phase transition temperature of the second phospholipid ranges from – 20 to 4°C.

Claim 23 (Previously presented): The formulated liposome according to claim 21, wherein the first phospholipid is a phosphatidyl choline (PC) and is selected from the group consisting of hydrogenated egg phosphatidyl choline (HEPC), hydrogenated soy phosphatidyl choline (HSPC), dipalmitoyl phosphatidyl choline (DPPC) and distearyllyl phosphatidyl choline (DSPC),

Claim 24 (Previously presented): The liposome according to claim 21, wherein the second phospholipid is a phosphatidyl choline (PC) and is selected from the group consisting of egg phosphatidyl choline (EPC), soy phosphatidyl choline (SPC), synthetic or natural-occurring unsaturated phosphatidyl choline and dilauroyl phosphatidyl choline (DLPC), oleoyl palmitoyl phosphatidyl choline, dioleoyl phosphatidyl choline, and dipetroselinoyl phosphatidyl choline, dipalmitelaidoyl phosphatidyl choline.

Claim 25 (Previously presented): The formulated liposome according to claim 21, wherein the hydrophobic substances are one or more hydrophobic pharmaceutical compounds.

Claim 26 (Currently amended): The formulated liposome according to claim 25, wherein the one or more hydrophobic pharmaceutical compound is ~~at least one of paclitaxel and a paclitaxel derivative~~.

Claim 27 (Currently amended): The formulated liposome according to claim 26, wherein the ~~at least one of paclitaxel and a paclitaxel derivative~~ is incorporated with a drug/lipid ratio ranging from at least 20 ~~about 0.5~~ mole% to 25 mole%.

Claim 28 (Currently amended): The formulated liposome according to claim 27, wherein the ~~at least one of paclitaxel and a paclitaxel derivative~~ is incorporated with a drug/lipid ratio ranging from at least 20 ~~about 0.5~~ mole% to 25 mole% when the first phospholipid is hydrogenated egg phosphatidyl choline (HEPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 29 (Currently amended): The formulated liposome according to claim 27, wherein the ~~at least one of paclitaxel and a paclitaxel derivative~~ is incorporated with a drug/lipid ratio ranging from at least 20 ~~about 0.5~~ mole% to 25 mole% when the first phospholipid is hydrogenated soy phosphatidyl choline (HSPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 30 (Currently amended): The formulated liposome according to claim 25, wherein the one or more hydrophobic pharmaceutical compound is ~~at least one of retinoic acid and a retinoic acid derivative~~.

Claim 31 (Currently amended): The formulated liposome according to claim 30, wherein the ~~at least one of retinoic acid and a retinoic acid derivative~~ is incorporated with a drug/lipid ratio ranging from at least 20 ~~about 0.5~~ mole% to 40 mole%.

Claim 32 (Currently amended): The formulated liposome according to claim 31, wherein the ~~at least one of retinoic acid and a retinoic acid derivative~~ is incorporated with a drug/lipid ratio ranging from at least 20 ~~about 10~~ mole% to 40 mole% when the first

phospholipid is hydrogenated soy phosphatidyl choline (HSPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 33 (Currently amended): The formulated liposome according to claim 25, wherein the one or more hydrophobic pharmaceutical compound is ~~at least one of~~ camptothecin ~~and a camptothecin derivative~~.

Claim 34 (Currently amended): The formulated liposome according to claim 33, wherein the ~~at least one of~~ camptothecin ~~and a camptothecin derivative~~ is incorporated with a drug/lipid ratio ranging from at least 20 ~~about 5~~ mole% to 30 mole%.

Claim 35 (Currently amended): The formulated liposome according to claim 34, wherein the ~~at least one of~~ camptothecin ~~and a camptothecin derivative~~ is incorporated with a drug/lipid ratio ranging from at least 20 ~~about 5~~ mole% to 30 mole% when the first phospholipid is hydrogenated egg phosphatidyl choline (HEPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 36 (Currently amended): The formulated liposome according to claim 25, wherein the one or more hydrophobic pharmaceutical compound is selected from the group consisting of ~~at least one of~~ paclitaxel ~~and a paclitaxel derivative~~, ~~at least one of~~ retinoic acid ~~and a retinoic acid derivative~~, and ~~at least one of~~ camptothecin ~~and a camptothecin derivative~~.

Claim 37 (Currently amended): The formulated liposome according to claim 21, wherein the liposome-forming materials are selected from the group consisting of hydrophilic polymer-modified lipids, cholesterol, ~~cholesterol derivatives~~, antioxidant, and mixture thereof.

Claim 38 (Previously presented): The formulated liposome according to claim 37, wherein the hydrophilic polymer-modified lipid is methoxy polyethylene glycol-distearoyl phosphatidyl ethanolamine (MPEG-DSPE).

Claim 39 (Currently amended): The formulated liposome according to claim 1, wherein the one or more hydrophobic substances incorporated in the liposome is present in an amount of ranging from at least 20 ~~about 3~~ mole% to about 25 mole%.

Claim 40 (Currently amended): The formulated liposome according to claim 1, wherein the one or more hydrophobic substances incorporated in the liposome is present in an amount ranging from at least 20 ~~about 8~~ mole% to about 25 mole.

Claim 41 (Cancelled).

Claim 42 (Currently amended): The formulated liposome according to claim 21, wherein the one or more hydrophobic substances incorporated in the liposome is present in an amount ranging from at least 20 ~~about 3~~ mole% to about 25 mole%.

Claim 43 (Currently amended): The formulated liposome according to claim 21, wherein the one or more hydrophobic substances incorporated in the liposome is present in an amount ranging from at least 20 ~~about 8~~ mole% to about 25 mole%.

Claim 44 (Cancelled).

Claim 45 (Previously presented): The formulated liposome according to claim 1, wherein the first and second phospholipids are phosphatidyl cholines.

Claim 46 (Previously presented): The formulated liposome according to claim 21, wherein the first phospholipid and the second phospholipid are present in a molar ratio of the first phospholipid to the second phospholipid is at least 3:16.